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MDR ACINETOBACTER INFECTIONS: AN ALARMING THREAT FOR CRITICALLY ILL PATIENTS

Gopal Kumar*

Senior Resident Microbiology, Trauma Centre, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.

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***Correspondence for Author**
Gopal Kumar
Senior Resident Microbiology, Trauma Centre, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.

ABSTRACT

Acinetobacter are a group of non-fermentative, Gram-negative cocco-bacilli bacteria that have minimal nutritional requirements and can survive on a variety of surfaces and aqueous environments. At present *Acinetobacter* is a growing public health threat affecting a considerable proportion of critically ill patients in several parts of the world. There has been increasing concern regarding the rise of *Acinetobacter* infections in critically ill patients. Infections caused by *A. baumannii* are associated with higher mortality and morbidity because of its relatively high virulence and antimicrobial resistance. *Acinetobacter* is a formidable challenge to managing these critically ill patients. *Acinetobacter* has become one of the leading cause of nosocomial infection because of the genetic capabilities to acquire resistance and partly due to high selective pressure, especially in critical care units. This pathogen's ability to rapidly develop antimicrobial resistance to all currently available antimicrobial agents is concerning because increasing data support attributable mortality to these bacteria when associated with hospitalized patients with comorbidities and severe illness. It disseminates antibiotic resistance by virtue of its extraordinary ability to accept or donate resistance plasmids. These infections most frequently involve the respiratory tract of intubated patients. The role of dual therapy is currently unclear and might be associated with increased toxicities without proven synergy or ability to prevent the development of resistance. Infection control and antibiotic control measures might have the greatest impact on these bacteria. Continued efforts are needed to develop new antimicrobial agents against this pathogen and assess the ideal amongst currently available agents.

IMPORTANCE

Once it was considered as a pathogen of low virulence but the recent evidences have shown it to be an important nosocomial pathogen. *Acinetobacter* is currently an important cause of nosocomial infections, including HAP and ventilator associated pneumonia (VAP) particularly in ICUs. Infections most frequently involve the respiratory tract, particularly of intubated patients. However, *Acinetobacter* is also a common cause of urinary tract and wound infections in ICU patients and on occasion local infections can progress to bacteraemia as well.

TAXONOMY

Acinetobacter spp. Are oxidase-negative, catalase-positive, indole-negative, and nitrate-negative. They can grow on ordinary microbiology culture media. Some strains produce acid from D-glucose, D-ribose, D-xylose, and L-arabinose (which are utilized oxidatively as carbon sources).

Although variants appear, typical colonies are smooth, dome shaped pale yellow to greyish, around 2 mm in diameter with entire edge. Most species grow at ambient temperature, and pathogenic species such as *A.baumannii* can grow well at 37℃.The genus *Acinetobacter* is now classified in the family *Moraxillaceae*, which includes Moraxella, Acinetobacter, Psychrobacter, and related organisms.[1] *Acinetobacter* uses a wide variety of organic compounds as a source of carbon and this property has been used in developing different identification system for this organism.

HABITAT AND COLONIZATION

Although not much is known about the natural reservoir and habitat of *Acinetobacter* spp, they are commonly present in soil and water as free-living saprophytes and some of these pathogenic *Acinetobacter* constitute to the normal flora of human skin, upper respiratory and gastrointestinal tract. Many of these can cause moderate to severe infections.

Acinetobacter baumannii along with two other genetically related species contribute to major human infections. This group is known as *Acinetobacter baumannii-Acinetobacter calcocaceticus* complex (*Abc* complex).

EPIDEMIOLOGY

Acinetobacter are widely distributed in nature and can be isolated from soil and fresh-water samples, as well as from humans and animals. Certain *Acinetobacter* spp., chiefly *A. johnsonii*, *A. lwoffii* and *A. radioresistens*, are part of the bacterial flora of the skin, where they are found predominantly in moist skin areas. In contrast, it is believed *A. baumannii* is usually isolated from patients and hospital environmental sources. *Acinetobacter* can cause a wide array of infections such as respiratory tract infections, bloodstream infections, urinary tract infections, meningitis, endocarditis and wound infections. *A. baumannii* is an excellent colonizer and is known to form biofilms. Furthermore, the reports demonstrate a positive correlation between biofilm formation capabilities and the multidrug resistance (MDR) status of *A. baumannii*. Such phenotypes have the ability to mediate outbreaks.[2]

Risk factors for colonization and infection with *A. baumannii* include major surgery, trauma, burns, previous hospitalization, stay in an ICU, length of hospital stay or ICU stay, mechanical ventilation, indwelling foreign devices (e.g., intravascular catheters, urinary catheters and drainage tubes), the number of invasive procedures performed, and previous antimicrobial therapy.[3]

Lack of infection control guidelines and the use of broad-spectrum antibiotics especially carbapenems and third-generation cephalosporins are major factors for the development of an MDR phenotype in *A. baumannii*.[4]

SOURCES OF INFECTION

A. baumannii infections can be acquired through endogenous or exogenous routes. Most frequently, the infection is exogenous in origin because of the ability of the organisms to survive longer in the environment and on dry surfaces and because they are resistant to desiccation. *A. baumannii* can multiply not only on human and animal skin, but also in soil and water and thus have a diversity of reservoirs. *A. baumannii* have been found include ventilator tubing, suction catheters, humidifiers, containers of distilled water, urine collection jugs, intravenous nutrition, multidose vials of medication, potable water, moist bedding articles, pillows, and inadequately sterilized reusable arterial pressure transducers.[5,6,7]

A. baumannii have been found in or on water taps, sinks, and computer keyboards and on all other inanimate surfaces that can act as a reservoir.[8,9] The mode of infection can be environmental contamination or cross contamination.

RISK FACTORS AND NOSOCOMIAL ACQUISITION

In addition to weakened immune system, chronic and debilitating disease and Diabetes other several factors associated may increase the risk of nosocomial infection with *A. baumannii*. Most important among them are mechanical ventilation (source of VAP), intensive care and other critical care units, wound and burn units, prolonged hospital stay, prior antibiotic therapy, increased exposures to infected patients, colonized neighbouring patients, and health care personnel. Infections and outbreaks in the long-term care facilities or nursing homes have been more commonly reported recently.[10] Most have been attributed to *A. baumannii,* particularly in the ICU setting, and to a lesser extent to *A. nosocomialis* and *A. pittii*. On the basis of the rising incidence of community-acquired *A. baumannii* infection, a concurrent spread of multidrug resistance is the greatest risk.

METHODS TO CONTROL INFECTION

Once endemic in any healthcare unit, MDR *A. baumannii* are extremely difficult to eradicate and control. The incorporation of a range of enhanced measures with the commitment at all levels including of healthcare personnel will be needed for its control. Identifying the source of transmission, timely feedback of information, cleaning of environment and disinfection of medical equipment, reinforcement of hand hygiene and standard precaution are all required. Closed tracheal suction system for all patients receiving mechanical ventilation is advised to prevent contamination and the provision of isolation of infected patient should be done.

Selective decontamination of skin with chlorhexidine reduced a significant load of *A. baumannii* and has been proposed as the infection control measure to lower the number of endemic outbreaks.[11]

RESISTANCE IN *ACINETOBACTER*

Infection caused by *A. baumannii* is often severe and difficult to treat due to high rates of resistance among clinical strains to major antibiotic classes. This organism is a known reservoir of multiple plasmids carrying antibiotic resistance markers.

Failure to maintain hospital hygiene, selective pressure due to irrational use of antibiotics, and mobile genetic elements encoding the bacterial resistance mechanism are the major forces for resistance development.[12] The resistance among *A. baumannii* strains to β-lactam agents is of great concern among clinicians. The susceptibility to polymyxins or Tigecycline now remains acceptable according to recent antimicrobial susceptibility pattern. Combination

therapy is suggested when the infections caused by *A. baumannii* are non-susceptible to all conventional drugs available.

Of concern is the fact that increasing use of polymyxins to treat *A. baumannii* infections in critically-ill patients may lead rapidly to the emergence of resistance.[13] and heteroresistance of *A. baumannii* isolates to colistin has also been described.[14,15]

CONCLUSION

At present there is no new drug in pharmaceutical pipeline or none of the FDA-approved antimicrobial compounds tested that has appreciable effect in control of MDR *A. baumannii*. Continued efforts are needed to develop new antimicrobial agents against this pathogen and assess the ideal amongst the currently available agents.

Constant efforts are to be made to contain the dissemination and hospital outbreaks to control this multidrug resistant *Acinetobacter* infection and we need new drugs or at least a rational combination therapy.

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